

Period Variability of Coupled Noisy Oscillators

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Abstract

Period variability, quantified by the standard deviation (SD) of the cycle-to-cycle period, is investigated for noisy phase oscillators. We define the checkpoint phase as the beginning/end point of one oscillation cycle and derive an expression for the SD as a function of this phase. We find that the SD is dependent on the checkpoint phase only when oscillators are coupled. The applicability of our theory is verified using a realistic model. Our work clarifies the relationship between period variability and synchronization from which valuable information regarding coupling can be inferred.

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Oscillators functioning as clocks, such as crystal oscillators [1], spin torque oscillators [2–5], and circadian and heart pacemakers [6–8], play an important role in various systems. Although these clocks are subjected to various types of noise, including thermal, quantum, and molecular noise, they are required to perform temporally precise oscillations; i.e., oscillations with only a small variability in the period (known as “period jitter” in electronic engineering [9]).

In many cases, it is sufficient for the clock to strike precisely at a specific time in each oscillation cycle, and thus a perfectly regular oscillation waveform is not needed. For cardiac pacemakers only the moment of stimulation is relevant. Experimental data regarding circadian activity in mice [10] indicate that the variability in the period between each activity onset is smaller than that between each offset. Similar results have also been obtained in explant circadian pacemaker tissue (the suprachiasmatic nucleus, SCN) [10]. These observations suggest that the onset is more important than the offset in a circadian clock, which may be designed in such a way that the crucial moment is expressed with high precision.

Remember that the definition of an oscillation period requires a fixed beginning/end point for each oscillation cycle; hereafter referred to as the checkpoint (Fig. 1). Although the average period does not depend on the particular choice of checkpoint, the period variability may be sensitive to the checkpoint. In order to clarify whether the checkpoint dependence in circadian activity is an artifact due to a technical problem in determining the onset and offset times or an essential property of the circadian clock, we need to investigate under what conditions the period variability is dependent on the checkpoint; this has received scant attention to date.

Another important aspect of the period variability is its relationship to synchronization. A clock is commonly synchronized to its master clock such as in the case of the SCN in response to the daily variation of sunlight, and in peripheral clocks in response to the SCN. In addition, most biological clocks, including the SCN, cardiac pacemakers, and pacemakers in weakly electrical fish, are composed of a population of synchronized oscillators [6, 7, 11]. It is known, both experimentally and theoretically, that period variability is reduced when the oscillators are coupled and synchronized [6, 12–16]. The question, therefore, arises as to whether the checkpoint dependence of the period variability is attributable to the interaction between oscillators.

In this Letter, we discuss this checkpoint dependence for the case of coupled noisy phase

oscillators. The period variability can be quantified using the standard deviation (SD) of the cycle-to-cycle period, and we show that although the SD is not dependent on the checkpoint in a single phase oscillator, it is dependent in a system of coupled phase oscillators; i.e., the checkpoint dependence results from the coupling effect. The SD is derived as a function of the checkpoint phase, which clarifies the relationship between the SD and synchronization. In particular, we find that in the case of diffusive coupling between oscillators, the checkpoint dependence of the SD has the same tendency as that of the synchronization: the SD is small when the oscillators are well synchronized. In other cases, however, the relationship is more complex. We also apply our theory to a realistic model of the electrical activity in a cell to demonstrate its validity. We believe that this is the first theoretical study to elucidate the existence of precise timing and its relationship with synchronization.

To begin, we prove that the period variability is independent of the checkpoint in a single phase oscillator system. When a limit cycle oscillator is subjected to weak noise, its dynamics are well described by the following phase oscillator model [17, 18];

$$\frac{d\theta}{dt} = \omega + Z(\theta)\sqrt{D}\xi(t), \quad (1)$$

where θ and ω are the phase and natural frequency, respectively. The 2π -periodic function $Z(\theta)$ is a phase sensitivity function, which quantifies the phase response of the oscillator to noise, and $\xi(t)$ denotes independent and identically distributed (i.i.d.) noise; each random variable $\xi(t)$ for all t obeys the same probability distribution and all are mutually independent. The positive constant D denotes the noise strength. Note that our proof below holds even if we permit ω and the probability distribution of ξ to be 2π -periodic functions of θ : $\omega(\theta)$ and $\xi(t, \theta)$.

The k th oscillation time of an oscillator, $t_k^{\theta_{\text{cp}}}$, is defined as the time at which θ passes through $2\pi k + \theta_{\text{cp}}$ ($0 \leq \theta_{\text{cp}} < 2\pi$) for the first time [Fig. 1(b)]. We define θ_{cp} as the checkpoint phase. The k th oscillation period $\Delta t_k^{\theta_{\text{cp}}}$ is defined as $\Delta t_k^{\theta_{\text{cp}}} = t_k^{\theta_{\text{cp}}} - t_{k-1}^{\theta_{\text{cp}}}$, and the SD is defined as

$$\text{SD}(\theta_{\text{cp}}) = \sqrt{E[(\Delta t_k^{\theta_{\text{cp}}} - \tau)^2]}, \quad (2)$$

where $E[\dots]$ represents the statistical average over k , and τ is the average period given by $\tau = E[\Delta t_k^{\theta_{\text{cp}}}]$. Note that $E[\dots]$ denotes both the statistical average taken over k and the ensemble average in the present paper, which are identical in the steady state. The system given by Eq. (1) is always in the steady state.

To prove that the SD is independent of θ_{cp} , we introduce two checkpoint phases denoted by α and β [Fig. 1(b)]. Since the processes $\alpha \rightarrow \beta$ and $\beta \rightarrow \alpha$ for any k are independent, we arrive at $\text{SD}(\alpha) = \text{SD}(\beta)$ for any arbitrary checkpoint phases α and β . A detailed proof is given in Appendix A.

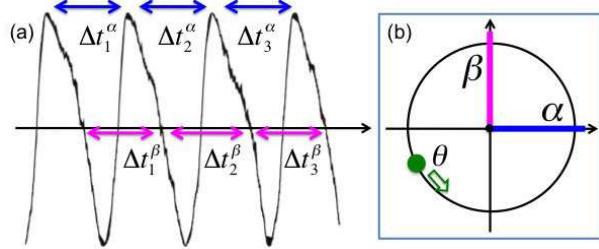


FIG. 1. (color online). (a) An example of the time series of an oscillation. Periods are observed at two checkpoints, α and β . (b) The corresponding checkpoint phases in the phase description.

Next, we consider a pair of coupled phase oscillators subjected to noise. When limit cycle oscillators are weakly coupled to each other and subjected to weak noise, the dynamics can be described by [17, 18]

$$\begin{cases} \dot{\theta}_1 = \omega + \kappa J(\theta_1, \theta_2) + Z(\theta_1)\sqrt{D}\xi_1(t), \\ \dot{\theta}_2 = \omega + \kappa J(\theta_2, \theta_1) + Z(\theta_2)\sqrt{D}\xi_2(t), \end{cases} \quad (3)$$

where θ_i and $\kappa \geq 0$ are the phase of the oscillator i and the coupling strength, respectively. The i.i.d. noise $\xi_i(t)$ satisfies $E[\xi_i(t)] = 0$ and $E[\xi_i(t)\xi_j(t')] = \delta_{ij}\delta(t - t')$. The 2π -periodic function $J(x, y)$ describes the interaction between oscillators, which leads to synchronization. We assume that, in the absence of noise ($D = 0$), the oscillators are synchronized in phase, i.e., $\theta_{1,2}(t) \rightarrow \phi(t)$ ($t \rightarrow \infty$), where $\phi(t)$ is a solution of

$$\dot{\phi}(t) = \omega + \kappa J(\phi, \phi). \quad (4)$$

The necessary condition for the stability of in-phase synchrony for $D = 0$ is provided below [see Eq. (11)]. We also assume that $\omega + \kappa J(\phi, \phi) > 0$ for any ϕ for the coupled system to be oscillatory.

Our particular interest is in the relationship between the SD [Eq. (2)] and the synchronization of two oscillators. We thus introduce the following order parameter that measures the phase distance from the in-phase state:

$$d(\theta_{\text{cp}}) = \sqrt{E [\|\theta_1 - \theta_2\|^2]_{\theta_1=\theta_{\text{cp}}}}, \quad (5)$$

where $E[x(t)]_{\theta_1=\theta_{\text{cp}}}$ represents the average of x_k over k (where x_k is the value of $x(t)$ taken when θ_1 passes through $2\pi k + \theta_{\text{cp}}$ for the first time), and $\|\theta_1 - \theta_2\|$ is the phase difference defined on the ring $[-\pi, \pi]$. The phase distance $d(\theta_{\text{cp}})$ is zero when the oscillators are completely synchronized in phase, and increases with the phase difference.

As we demonstrate below, the relationship between $\text{SD}(\theta_{\text{cp}})$ and $d(\theta_{\text{cp}})$ is qualitatively different for the two cases where $J(\phi, \phi)$ is (A) independent of ϕ and (B) dependent on ϕ . Cases (A) and (B) imply that $\dot{\phi}$ given in Eq. (4) is independent of ϕ and dependent on ϕ , respectively. Phase reduction theory indicates that it is appropriate to assume the form $J(x, y) = z(x)G(x, y)$, where $z(x)$ is the phase sensitivity function for the interaction $G(x, y)$ [17, 18]. It is known that diffusive coupling between chemical oscillators and gap-junction coupling between cells yields $J(x, y) = z(x)(h(x) - h(y))$, where h represents a chemical concentration [19, 20] or membrane potential, which corresponds to case (A). Case (A) also allows the form $J(x, y) = j(x - y)$, which has been employed in many models such as the Kuramoto model [18]; however, we do not employ this form in the demonstration, since the term $j(x - y)$ is derived as a result of averaging the interaction $z(x)G(x, y)$ over one oscillation period [18], and, by this approximation, the information about the θ_{cp} dependence is lost. Many other types of coupling, such as $J(x, y) = z(x)h(y)$ employed below, correspond to case (B) [21].

As an example of case (A), we consider $z(\theta) = \sin \theta$ for $0 \leq \theta < \pi$, $z(\theta) = 0$ for $\pi \leq \theta < 2\pi$, and $h(\theta) = \cos \theta$, and the following as an example of case (B): $z(\theta) = -\sin \theta$ and $h(\theta) = 1 + \cos \theta$ [21]. We set $Z(\theta) = 1$, $\omega = 2\pi$, $\sqrt{D} = 0.03 \times 2\pi$, and $\theta_1(0) = \theta_2(0) = 0$, and assume $\xi_{1,2}(t)$ to be white Gaussian noise. We integrate Eq. (3) using the Euler scheme with a time step of 5×10^{-4} for $t = 0$ – 10100 and discard the $t = 0$ – 100 data as transient.

Using these examples, numerically obtained SD values for θ_1 are plotted as a function of θ_{cp} in Fig. 2(a) and (b). The results indicate clearly the existence of θ_{cp} dependence in both cases, which was absent in the single phase oscillator system. This dependence becomes stronger for larger κ values. In contrast, for $\kappa \ll \omega$, the dependence vanishes because $J(x, y)$ is well approximated by $j(x - y)$ [18], and thus, the system effectively has rotational symmetry. The θ_{cp} value at which $\text{SD}(\theta_{\text{cp}})$ assumes its minimum represents the most precise timing.

The θ_{cp} dependence of $d(\theta_{\text{cp}})$ for the two cases is shown in Fig. 2 (c) and (d). A comparison with $\text{SD}(\theta_{\text{cp}})$ shows that the checkpoint phase maxima and minima of each

κ value coincide in the case of (A). Thus, the most precise timing is obtained when the oscillators are synchronized. By contrast, the θ_{cp} dependence is considerably different in the case of (B). Therefore, we expect that nontrivial factors, apart from synchronization, influence the SD. We also examined several other functions, $z(\theta)$, $h(\theta)$, and $Z(\theta)$, and found a similar relationship between $\text{SD}(\theta_{\text{cp}})$ and $d(\theta_{\text{cp}})$ (data not shown).

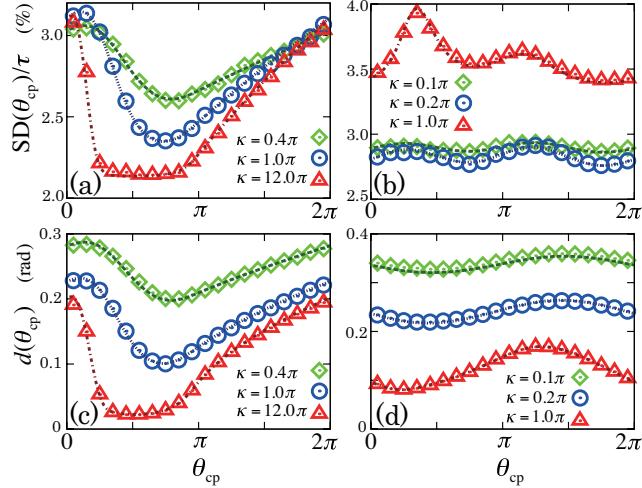


FIG. 2. (color online). The $\text{SD}(\theta_{\text{cp}})/\tau$ for case (A) and (B) is shown in (a) and (b), respectively, where the vertical scale is expressed as a percentage. The distance from in-phase synchronization, $d(\theta_{\text{cp}})$, for case (A) and (B) is shown in (c) and (d), respectively. The points and lines are the numerical results of the simulation and analytical predictions given by Eqs. (16) and (13), respectively.

We now derive an expression for the SD. The derivation consists of two steps: (i) calculation of the phase diffusion $\sigma(\theta_{\text{cp}})$ [defined by Eq. (7)] with a linear approximation, and (ii) transformation from $\sigma(\theta_{\text{cp}})$ to $\text{SD}(\theta_{\text{cp}})$. Here, we employ the solution $\phi(t)$ of Eq. (4) with $\phi(0) = 0$ and the time t_{cp} is defined by $\phi(t_{\text{cp}}) = \theta_{\text{cp}}$. The oscillation period for $D = 0$ is denoted by τ ; i.e., $\phi(t_{\text{cp}} + \tau) = \theta_{\text{cp}} + 2\pi$. After a transient time, our system approaches the steady state, which is defined by the following equation for all Ψ :

$$P(\|\theta_1 - \theta_2\|; \theta_1 = \Psi) = P(\|\theta_1 - \theta_2\|; \theta_1 = \Psi + 2\pi), \quad (6)$$

where $P(\|\theta_1 - \theta_2\|; \theta_1 = \Psi)$ is the probability density function of the distance $\|\theta_1 - \theta_2\|$ at $\theta_1 = \Psi$. We assume that the system is in the steady state at $t = 0$. The ensemble we consider here is defined by the initial condition at $t = t_{\text{cp}}$, $\theta_1(t_{\text{cp}}) = \theta_{\text{cp}}$, and $\theta_2(t_{\text{cp}})$ is distributed in

$[\theta_1(t_{\text{cp}}) - \pi, \theta_1(t_{\text{cp}}) + \pi]$ according to Eq. (6). From this point, $E[\dots]$ represents the average taken over this ensemble. The phase diffusion $\sigma(\theta_{\text{cp}})$ is defined by

$$\sigma(\theta_{\text{cp}})^2 = E[(\theta_1(t_{\text{cp}} + \tau) - \theta_1(t_{\text{cp}}) - 2\pi)^2]. \quad (7)$$

We also assume that the noise intensity D is sufficiently small and that the other parameters and functions are of $O(1)$, so that the phase difference $\|\theta_1 - \theta_2\|$ is small in most cases in the steady state.

To calculate the phase diffusion, we decompose $\theta_{1,2}$ as $\theta_{1,2}(t) = \phi(t) + \Delta_{1,2}(t)$. We then consider the time duration $0 \leq t \leq O(\tau)$, in which $\Delta_{1,2}(t) \ll 1$ is expected in most cases because $D \ll 1$. Therefore, we can linearize Eq. (3). We define the two modes, $X = \Delta_1 + \Delta_2$ and $Y = \Delta_1 - \Delta_2$, which obey

$$(\dot{X}, \dot{Y}) = \kappa f_{X,Y}(\phi(t))(X, Y) + \xi_{X,Y}(t, \phi(t)), \quad (8)$$

where $f_X(\phi) \equiv \frac{\partial J}{\partial x}\Big|_{x=y=\phi} + \frac{\partial J}{\partial y}\Big|_{x=y=\phi} = \frac{dJ(\phi, \phi)}{d\phi}$, $f_Y(\phi) \equiv \frac{\partial J}{\partial x}\Big|_{x=y=\phi} - \frac{\partial J}{\partial y}\Big|_{x=y=\phi}$, and $\xi_{X,Y}(t, \phi(t)) \equiv \sqrt{D}Z(\phi(t))(\xi_1(t) \pm \xi_2(t))$. Note that $f_X(\phi) = 0$ for all ϕ in case (A). The solutions of Eq. (8) can be described as

$$(X, Y)(t) = \exp[+\kappa F_{X,Y}(\phi(t))] \times \left\{ (X, Y)(0) + \int_0^t \exp[-\kappa F_{X,Y}(\phi(t'))] \xi_{X,Y}(t', \phi(t')) dt' \right\}, \quad (9)$$

where $F_{X,Y}(\phi(t)) \equiv \int_0^t f_{X,Y}(\phi(t')) dt'$. Furthermore, because $f_X(\phi) = \frac{dJ(\phi, \phi)}{d\phi}$, we obtain

$$F_X(\phi(t)) = \frac{1}{\kappa} \ln \left(\frac{\dot{\phi}(t)}{\dot{\phi}(0)} \right). \quad (10)$$

For $\xi_Y = 0$, we obtain $F_Y(2\pi) = (1/\kappa) \ln(Y(\tau)/Y(0))$. Therefore, in the absence of noise, in-phase synchronization is stable if

$$F_Y(2\pi) \equiv c < 0. \quad (11)$$

The correlations, $E[X(t)^2]$, $E[Y(t)^2]$, and $E[X(t)Y(t)]$ are given in Appendix B. Since Eq. (6) can be rewritten as $P(|\Delta_1 - \Delta_2|; t) \cong P(|\Delta_1 - \Delta_2|; t + \tau)$, then $E[Y(t)^2] = E[Y(t + \tau)^2]$ holds approximately, leading to

$$E[Y(0)^2] = 2D \frac{\exp[2\kappa c]}{1 - \exp[2\kappa c]} \int_0^\tau Z(\phi(t'))^2 \exp[-2\kappa F_Y(\phi(t'))] dt'. \quad (12)$$

In addition, because $d(\theta_{\text{cp}})^2 = E[(\Delta_1(t_{\text{cp}}) - \Delta_2(t_{\text{cp}}))^2] = E[Y(t_{\text{cp}})^2]$, we obtain

$$d(\theta_{\text{cp}})^2 = \exp[2\kappa F_Y(\theta_{\text{cp}})] \times \left(E[Y(0)^2] + 2D \int_0^{\theta_{\text{cp}}} Z(\phi)^2 \exp[-2\kappa F_Y(\phi)] \frac{ds}{d\phi(s)} d\phi \right), \quad (13)$$

which is generally θ_{cp} -dependent even if $Z(\phi)$ is constant.

Using these correlations and Eq. (10), we obtain the following expression for the phase diffusion (See Appendix B)

$$\begin{aligned} \sigma(\theta_{\text{cp}})^2 &= E[(\Delta_1(t_{\text{cp}} + \tau) - \Delta_1(t_{\text{cp}}))^2] \\ &= C_1 \dot{\phi}(\theta_{\text{cp}})^2 + C_2 d(\theta_{\text{cp}})^2, \end{aligned} \quad (14)$$

where the $C_{1,2}$ are independent of θ_{cp} and are given by $C_1 = \frac{D}{2} \int_0^{2\pi} \frac{Z(\theta)^2}{\dot{\phi}(\theta)^3} d\theta$ and $C_2 = (1 - \exp[\kappa c])/2$. The C_1 term is an effective diffusion constant for the center of the two oscillators, which is half that of an uncoupled oscillator, and the C_2 term is associated with the stability of the synchronization.

To transform $\sigma(\theta_{\text{cp}})$ to $\text{SD}(\theta_{\text{cp}})$, we note that when the noise intensity is low, most of the trajectories of $\theta_1(t)$ are very close to the unperturbed trajectory $\phi(t)$ (see Appendix C). In such a case, the following relation approximately holds true:

$$\frac{\sigma(\theta_{\text{cp}})}{\text{SD}(\theta_{\text{cp}})} = \dot{\phi}(\theta_{\text{cp}}). \quad (15)$$

The same approximation (but for constant $\dot{\phi}$) was employed in Ref. [16] and verified numerically.

From Eqs. (B11) and (15), we finally arrive at

$$\text{SD}(\theta_{\text{cp}}) = \sqrt{C_1 + C_2 \frac{d(\theta_{\text{cp}})^2}{\dot{\phi}(\theta_{\text{cp}})^2}}. \quad (16)$$

The analytical results given by Eqs. (16) and (13) are in excellent agreement with the numerical results (Fig. 2). Although we have only discussed paired identical phase oscillators, our theory can easily be extended to other cases, e.g., N globally coupled (all-to-all) identical oscillators or a periodically driven noisy oscillator.

Equation (16) shows that the periodicity of $\text{SD}(\theta_{\text{cp}})$ is based on the synchronization $d(\theta_{\text{cp}})$ and phase velocity $\dot{\phi}(\theta_{\text{cp}})$. For case (A), since $\dot{\phi}(\theta_{\text{cp}})$ is constant, there is one-to-one correspondence between $\text{SD}(\theta_{\text{cp}})$ and $d(\theta_{\text{cp}})$; i.e., the most precise timing ($\theta_{\text{cp}}^{\min}$) is the timing

at which the best synchronization is achieved. This was observed in Fig. 2 (a) and (c), where $\theta_{\text{cp}}^{\min} = \pi/2 + O(\kappa^{-1})$ can be obtained from $dd(\theta_{\text{cp}})/d\theta_{\text{cp}} = 0$. For case (B), however, the SD also depends on $\dot{\phi}(\theta_{\text{cp}})$; this is in contrast to that observed for the single phase oscillator system in which the phase velocity $\omega(\theta)$ does not contribute to the checkpoint dependence of the SD. Figures 2(b) and (d) showed that $\text{SD}(\theta_{\text{cp}})$ and $d(\theta_{\text{cp}})$ are considerably different, which indicates the strong effect of $\dot{\phi}$ in this particular example. Indeed, $\text{SD}(\theta_{\text{cp}})$ assumes its minimum around a maximum $\dot{\phi}(\theta_{\text{cp}})$ ($\theta_{\text{cp}}^{\min} \approx 5\pi/3$).

To investigate whether Eq. (16) holds for a more realistic model, we employ the FitzHugh-Nagumo model given by

$$\begin{cases} \dot{V}_1 = V_1(V_1 - a)(1 - V_1) - W_1 + \xi_1(t) + K_V(V_2 - V_1), \\ \dot{W}_1 = \epsilon(V_1 - bW_1) + K_W(W_2 - W_1), \end{cases} \quad (17)$$

in which the second oscillator is described in a similar way. We fixed $a = -0.1$, $b = 0.5$, and $\epsilon = 0.01$. This system shows limit-cycle oscillations with a period of $\tau \simeq 126.5$ when noise and coupling are absent. The white Gaussian noise $\xi_i(t)$ has an intensity of 0.01. The interaction is diffusive, i.e., case (A), and we consider the following two types: V -coupling ($K_V = 0.01$, $K_W = 0$) and W -coupling ($K_V = 0$, $K_W = 0.01$). The phase θ was defined properly (see Appendix D), and $\text{SD}(\theta_{\text{cp}})$ and $d(\theta_{\text{cp}})$ were obtained numerically. Figure 3 shows that the θ_{cp} -dependence of the SD is different in the two cases, suggesting a significant effect from the coupling. We estimated the C_1 and C_2 values using Eq. (16) and the least-squares method under the condition that both cases have the same C_1 value, resulting in $C_1 = 5.4$, $C_2^{(V)} = 0.20$, and $C_2^{(W)} = 0.48$. In Fig. 3, we can see that the SD is described well by Eq. (16) using the fitted C_1 and C_2 values. This demonstrates that the theory is valid for this biological model.

In many cases, only the SD measured at a functionally relevant checkpoint characterizes the performance of a clock. When designing a precise clock, we only have to reduce $\text{SD}(\theta_{\text{cp}})$ for a specific θ_{cp} . Equation (16) implies that $\text{SD}(\theta_{\text{cp}})$ at a given θ_{cp} decreases with decreasing $d(\theta_{\text{cp}})$ and increasing $\dot{\phi}(\theta_{\text{cp}})$. Therefore, attractive coupling between oscillators should be activated around the functionally relevant timing point. In addition, in case (B), the phase velocity should be increased through coupling.

Our theory enables us to infer the coupling timing or form by measuring $\text{SD}(\theta_{\text{cp}})$ at several checkpoints. Although this is, in principle, possible with $d(\theta_{\text{cp}})$, using $\text{SD}(\theta_{\text{cp}})$ has the added advantages that the SD can be measured from a single time series and that $d(\theta_{\text{cp}})$

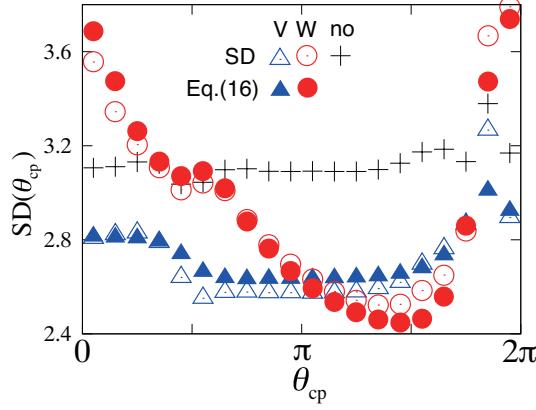


FIG. 3. (color online). Validation of Eq. (16) in the FitzHugh-Nagumo model. Open symbols are the numerically obtained SD values. Filled symbols are the SD values evaluated from Eq. (16) with the numerically obtained d values and fitting parameters C_1 and C_2 . The triangles and circles represent the V - and W -coupling cases. The plus symbols are the numerically obtained SD values for an uncoupled oscillator.

is sensitive to the definition of phase. From the observations of circadian periods in mice described in the introduction [10], it is possible that the SCN sends signals to the peripheral clocks around the onset of a subjective day. An experimental observation of the checkpoint dependence in other biological clocks would be a new source of coupling information.

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Appendix A: Proof that the SD is independent of the checkpoint phase in a single phase oscillator

We introduce two checkpoint phases denoted by α and β . By defining the intervals $\Delta t_k^{\beta \rightarrow \alpha} = t_k^\alpha - t_k^\beta$ and $\Delta t_k^{\alpha \rightarrow \beta} = t_k^\beta - t_{k-1}^\alpha$, the oscillation periods observed at α and β can be decomposed as $\Delta t_k^\alpha = \Delta t_k^{\beta \rightarrow \alpha} + \Delta t_k^{\alpha \rightarrow \beta}$ and $\Delta t_k^\beta = \Delta t_k^{\alpha \rightarrow \beta} + \Delta t_{k-1}^{\beta \rightarrow \alpha}$, respectively. Because $\xi(t)$ is independent, the processes $\alpha \rightarrow \beta$ and $\beta \rightarrow \alpha$ for any k are independent. We thus have

$$E[\Delta t_k^{\beta \rightarrow \alpha}] = E[\Delta t_{k-1}^{\beta \rightarrow \alpha}], \quad (\text{A1})$$

$$E[(\Delta t_k^{\beta \rightarrow \alpha})^2] = E[(\Delta t_{k-1}^{\beta \rightarrow \alpha})^2], \quad (\text{A2})$$

and

$$E[\Delta t_k^{\alpha \rightarrow \beta} \Delta t_{k-1}^{\beta \rightarrow \alpha}] = E[\Delta t_k^{\alpha \rightarrow \beta}] E[\Delta t_{k-1}^{\beta \rightarrow \alpha}] = E[\Delta t_k^{\alpha \rightarrow \beta} \Delta t_k^{\beta \rightarrow \alpha}]. \quad (\text{A3})$$

The average and the mean square period are independent of the checkpoint phase labels; i.e.,

$$E[\Delta t_k^\alpha] = E[\Delta t_k^{\beta \rightarrow \alpha}] + E[\Delta t_k^{\alpha \rightarrow \beta}] = E[\Delta t_{k-1}^{\beta \rightarrow \alpha}] + E[\Delta t_k^{\alpha \rightarrow \beta}] = E[\Delta t_k^\beta] = \tau \quad (\text{A4})$$

and

$$E[(\Delta t_k^\alpha)^2] = E[(\Delta t_k^{\beta \rightarrow \alpha})^2] + E[(\Delta t_k^{\alpha \rightarrow \beta})^2] + 2E[\Delta t_k^{\beta \rightarrow \alpha}][\Delta t_k^{\alpha \rightarrow \beta}] = E[(\Delta t_k^\beta)^2]. \quad (\text{A5})$$

Thus, we arrive at

$$\text{SD}(\alpha) = \sqrt{E[(\Delta t_k^\alpha - \tau)^2]} = \sqrt{E[(\Delta t_k^\beta - \tau)^2]} = \text{SD}(\beta) \quad (\text{A6})$$

for any arbitrary checkpoint phases α and β .

Appendix B: Calculation of the correlations

The correlations of the noise terms, $\xi_{X,Y}(t, \phi(t)) = \sqrt{D}Z(\phi(t))(\xi_1(t) \pm \xi_2(t))$, are given as

$$E[\xi_X(s, \phi(s))\xi_X(s', \phi(s'))] = 2DZ(\phi(s))Z(\phi(s'))\delta(s - s'), \quad (\text{B1})$$

$$E[\xi_Y(s, \phi(s))\xi_Y(s', \phi(s'))] = 2DZ(\phi(s))Z(\phi(s'))\delta(s - s'), \quad (\text{B2})$$

$$E[\xi_X(s, \phi(s))\xi_Y(s', \phi(s'))] = 0. \quad (\text{B3})$$

Using Eqs. (9), (B1), (B2), (B3), and $E[\xi_{X,Y}(t, \phi(t))] = 0$, we obtain

$$\begin{aligned} E[X(t)^2] &= \exp[2\kappa F_X(\phi(t))]\left[E[X(0)^2] \right. \\ &\quad \left. + \int_0^t \int_0^t \exp[-\kappa\{F_X(\phi(s)) + F_X(\phi(s'))\}]E[\xi_X(s, \phi(s))\xi_X(s', \phi(s'))]dsds'\right] \\ &= \exp[2\kappa F_X(\phi(t))]\left[E[X(0)^2] + 2D \int_0^t Z(\phi(s))^2 \exp[-2\kappa F_X(\phi(s))]ds\right], \end{aligned} \quad (\text{B4})$$

$$\begin{aligned} E[Y(t)^2] &= \exp[2\kappa F_Y(\phi(t))]\left[E[Y(0)^2] \right. \\ &\quad \left. + \int_0^t \int_0^t \exp[-\kappa\{F_Y(\phi(s)) + F_Y(\phi(s'))\}]E[\xi_Y(s, \phi(s))\xi_Y(s', \phi(s'))]dsds'\right] \\ &= \exp[2\kappa F_Y(\phi(t))]\left[E[Y(0)^2] + 2D \int_0^t Z(\phi(s))^2 \exp[-2\kappa F_Y(\phi(s))]ds\right], \end{aligned} \quad (\text{B5})$$

and

$$E[X(t)Y(t)] = \exp[\kappa(F_X(\phi(t)) + F_Y(\phi(t)))]E[X(0)Y(0)]. \quad (\text{B6})$$

Substituting $t = t_{\text{cp}} + \tau$ in Eqs. (B4) and (B6), we obtain

$$\begin{aligned} E[X(t_{\text{cp}} + \tau)^2] &= \exp[2\kappa F_X(\theta_{\text{cp}} + 2\pi)] \left[E[X(0)^2] + 2D \int_0^{t_{\text{cp}} + \tau} Z(\phi(s))^2 \exp[-2\kappa F_X(\phi(s))] ds \right] \\ &= \exp[2\kappa F_X(\theta_{\text{cp}})] \left[E[X(0)^2] + 2D \int_0^{t_{\text{cp}}} + \int_{t_{\text{cp}}}^{t_{\text{cp}} + \tau} Z(\phi(s))^2 \exp[-2\kappa F_X(\phi(s))] ds \right] \\ &= E[X(t_{\text{cp}})^2] + 2D \exp[2\kappa F_X(\theta_{\text{cp}})] \int_0^{\tau} Z(\phi(s))^2 \exp[-2\kappa F_X(\phi(s))] ds, \end{aligned} \quad (\text{B7})$$

and

$$\begin{aligned} E[X(t_{\text{cp}} + \tau)Y(t_{\text{cp}} + \tau)] &= \exp[\kappa(F_X(\theta_{\text{cp}} + 2\pi) + F_Y(\theta_{\text{cp}} + 2\pi))]E[X(0)Y(0)] \\ &= \exp[\kappa c]E[X(t_{\text{cp}})Y(t_{\text{cp}})], \end{aligned} \quad (\text{B8})$$

where we use $\phi(t_{\text{cp}} + \tau) = \theta_{\text{cp}} + 2\pi$, $F_X(\theta + 2\pi) = F_X(\theta)$, $F_Y(\theta + 2\pi) = F_Y(\theta) + c$, and $Z(\theta + 2\pi) = Z(\theta)$. Inserting $\theta_1(t_{\text{cp}}) = \theta_{\text{cp}}$ and $\phi(t_{\text{cp}}) = \theta_{\text{cp}}$ into the definition $\Delta_1(t) = \theta_1(t) - \phi(t)$, we obtain

$$\Delta_1(t_{\text{cp}}) = 0. \quad (\text{B9})$$

We then obtain

$$E[X(t_{\text{cp}})^2] = -E[X(t_{\text{cp}})Y(t_{\text{cp}})] = E[Y(t_{\text{cp}})^2] = d(\theta_{\text{cp}})^2. \quad (\text{B10})$$

Using Eqs. (B7)–(B10), the relation $E[Y(t_{\text{cp}} + \tau)^2] = E[Y(t_{\text{cp}})^2]$, and Eq.(10), we obtain the following expression for the phase diffusion

$$\begin{aligned} \sigma(\theta_{\text{cp}})^2 &= E[(\Delta_1(t_{\text{cp}} + \tau) - \Delta_1(t_{\text{cp}}))^2] \\ &= \frac{1}{4} \left\{ E[X(t_{\text{cp}} + \tau)^2] + E[Y(t_{\text{cp}} + \tau)^2] + 2E[X(t_{\text{cp}} + \tau)Y(t_{\text{cp}} + \tau)] \right\} \\ &= \frac{1}{4} \left\{ 2D \exp[2\kappa F_X(\theta_{\text{cp}})] \int_0^{\tau} Z(\phi(t'))^2 \exp[-2\kappa F_X(\phi(t'))] dt' + 2(1 - \exp[\kappa c])d(\theta_{\text{cp}})^2 \right\} \\ &= C_1 \dot{\phi}(\theta_{\text{cp}})^2 + C_2 d(\theta_{\text{cp}})^2. \end{aligned} \quad (\text{B11})$$

Appendix C: Transformation from phase diffusion to period variability

Here, we illustrate the relationship between $\sigma(\theta_{\text{cp}})$ and $\text{SD}(\theta_{\text{cp}})$. Figure 4(a) presents a schematic view of the trajectories of $\phi(t)$ and $\theta_1(t)$. An enlarged view of the region around $(t_{\text{cp}} + \tau, \theta_{\text{cp}} + 2\pi)$ is displayed in Fig. 4(b), in which the vertical width between the dotted lines represents the standard deviation of the phase distribution of $\theta_1(t)$. In particular, the vertical arrow represents the standard deviation of $\theta_1(t_{\text{cp}} + \tau)$, which is denoted by $\sigma(\theta_{\text{cp}})$. Because we assume a low noise intensity, the actual trajectories of $\theta_1(t)$ (thin lines) are very close to that of $\phi(t)$. We can thus expect that the trajectories are approximately straight and parallel to $\phi(t)$ in this enlarged region. Therefore, the horizontal width between the dotted lines at $\theta_1 = \theta_{\text{cp}} + 2\pi$ is approximately equal to $\text{SD}(\theta_{\text{cp}})$ (horizontal arrow), and the relation $\sigma(\theta_{\text{cp}})/\text{SD}(\theta_{\text{cp}}) = \dot{\phi}(\theta_{\text{cp}})$ holds approximately.

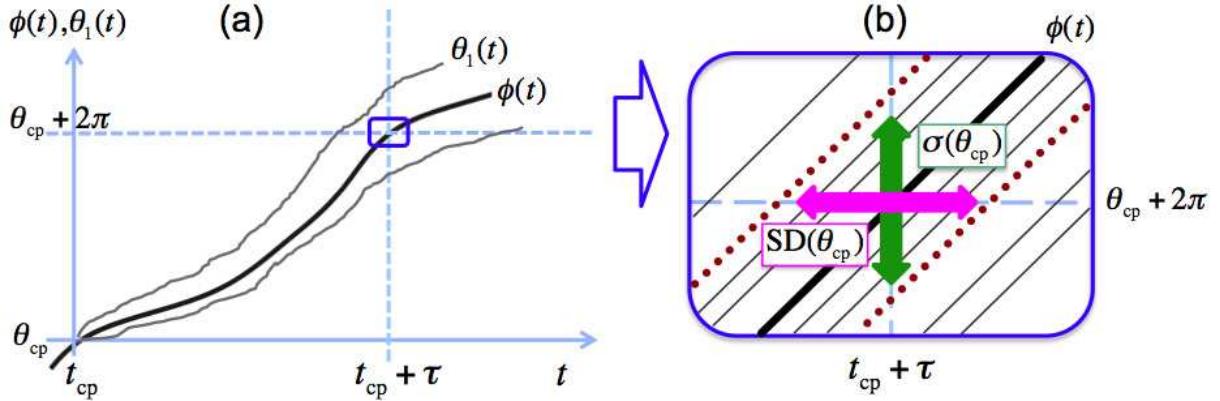


FIG. 4. Illustration of the relationship between $\sigma(\theta_{\text{cp}})$ and $\text{SD}(\theta_{\text{cp}})$.

Appendix D: Definition of phase in the FitzHugh-Nagumo model

We define the phase θ as a function of (V, W) , which are the state variables of the FitzHugh-Nagumo model given in Eq. (17) in the main text, as follows (Fig. 5). We first assign ϕ values to all points on the limit cycle trajectory generated by Eq. (17) without noise such that ϕ identically satisfies $\dot{\phi} = 2\pi/\tau$, where τ is the period. The limit cycle trajectory is independent of the coupling strengths. We set $\phi = 0$ at $V = 0.6$ with $\dot{V} > 0$. We then consider radial lines extending from an arbitrary point inside the limit cycle, which we chose as $(0.6, 0.05)$ (filled square) in this case. When a radial line intersects the limit cycle at a

point that has a value of ϕ , the phase θ of all points on the radial line is defined by $\theta = \phi$. These radial lines are different from isochrones that give a standard definition of the phase [18], but the isochrones are usually unknown. As shown in Fig. 3, our theory is valid even for this practical definition.

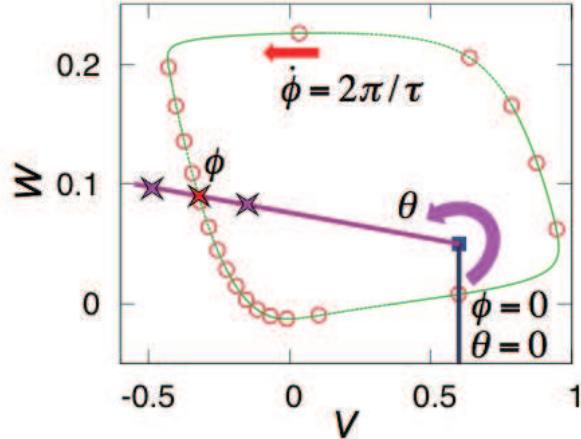


FIG. 5. Illustration of the definition of the phase in the FitzHugh-Nagumo model. The limit cycle trajectory is generated by a coupled FitzHugh-Nagumo model without noise, whose parameters are given in the main text. The circles are placed at equally spaced intervals of ϕ . All points on a straight line radiating from the origin (filled square) have the same phase.

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